NMR-SOLVE METHOD FOR RAPID IDENTIFICATION OF BI-LIGAND DRUG CANDIDATES

ABSTRACT

Methods for rapidly identifying drug candidates that can bind to an enzyme at both a common ligand site and a specificity ligand site, resulting in high affinity binding. The bi-ligand drug candidates are screened from a focused combinatorial library where the specific points of variation on a core structure are optimized. The optimal points of variation are identified by which atoms of a ligand bound to the common ligand site are identified to be proximal to the specificity ligand site. As a result, the atoms proximal to the specificity ligand site can then be used as a point for variation to generate a focused combinatorial library of high affinity drug candidates that can bind to both the common ligand site and the specificity ligand site. Different candidates in the library can then have high affinity for many related enzymes sharing a similar common ligand site.